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West German Patent No. 2,608,226 (Offenlegungsschrift)

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(54) AGENTS WITH A PHYSIOLOGICAL COOLING EFFECT

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CLAIMS

1. Agents with a physiological cooling effect on the skin and mucous membranes of the body, characterized in that they contain esters made from menthol and naturally occurring hydroxycarboxylic acids with 2 to 6 C atoms, which are optionally esterified, in turn, on the hydroxy group with carboxylic acids that have 1 to 4 C atoms.

2. Agents according to Claim 1, containing menthyl lactate as a cooling reagent.

3. Use of esters made from menthol and naturally occurring hydroxycarboxylic acids with 2 to 6 C atoms, which are optionally esterified, in turn, on the hydroxy group with carboxylic acids that have 1 to 4 C atoms, as agents with a physiological cooling effect on the skin and mucous membranes of the body.

4. Use of menthyl lactate according to Claim 3.

5. Cooling-agent-containing compositions characterized by a content of cooling agents in accordance with Claims 1 and 2.

6. Cooling-agent-containing compositions according to Claim 5, characterized in that they contain the cooling agents in accordance with Claims 1 and 2, in a quantity of 0.1 to 5 weight-percent, with reference to the weight of the preparation.

AGENTS WITH A PHYSIOLOGICAL COOLING EFFECT

The invention concerns agents with a physiological cooling effect on the skin and mucous membranes of the body.

Menthol, the main component of peppermint oils, is characterized by its excellent cooling effect on the skin and mucous membranes of the body. Its cooling effect is not based on the latent heat of evaporation, but rather is formed by the direct effect of the compound on the nerve endings of cold receptors. The odor and taste characteristics of menthol, however, limit its use and even make it impossible in some cases. The odor of peppermint is too specific and too sharp for different fields of application and are irritating to the lacrimal glands and mucous membranes. For other fields of application, the taste is too sharp and bitter. The great volatility of menthol often has a disadvantageous effect also.

There has been no lack of attempts, therefore, to find substances that have the positive effect of cooling, without the disadvantages of menthol described above. Thus, for example, West German Patent No. 2,202,535 (Offenlegungsschrift) proposes p-menthane-3-carboxamide and esters of p-methane-3-carboxylic acid; West German Patent No. 2,205,255 (Offenlegungsschrift) proposes N-substituted p-methane-3-carboxamides; West German Patent No. 2,317,538 (Offenlegungsschrift) proposes substituted amides; West German Patent No. 2,334,985 (Offenlegungsschrift) proposes cyclical and acyclical sulfoxides and sulfones; and West German Patent No. 2,345,156 (Offenlegungsschrift) proposes substituted phosphine oxides.

The compounds which, to some extent, greatly approximate the set goal of having a cooling effect, and thereby being odorless and tasteless, nevertheless have the disadvantage that they are neither naturally occurring substances nor can they be degraded by the human body to form naturally occurring substances. They are therefore of concern physiologically and with respect to food laws. Moreover, they are, in part, very expensive, since they can be produced only in processes with many stages.

The previously proposed derivatives of the menthol, which are either naturally occurring or are degraded by the organism to naturally occurring substances, only incompletely meet the requirements. Thus, the 1-menthylethyl carbonate proposed in West German Patent No. 2,022,364 (Offenlegungsschrift) has an orangelike odor; the N-acetylglycine menthyl ester, proposed in West German Patent No. 2,433,165 (Offenlegungsschrift) and the menthol ester of heterocyclic carboxylic

acids, proposed in West German Patent No. 2,339,661 (Offenlegungsschrift), are bitter; and the menthylketo esters proposed in U.S. Patent No. 3,830,930 are, in part, unremittingly bitter and do not exhibit the desired cooling effect.

It was then surprisingly discovered that esters made from menthol and naturally occurring hydroxycarboxylic acids with 2 to 6 C atoms, which are optionally esterified on the hydroxy group of the carboxylic acid, are odorless and tasteless and have an excellent, in particular, long-lasting cooling effect.

The invention therefore concerns agents with a physiological cooling effect on the skin and mucous membranes of the body, which are characterized in that they contain esters made from menthol and naturally occurring hydroxycarboxylic acids with 2 to 6 C atoms, which are optionally esterified, in turn, on the hydroxy group, with carboxylic acids that have 1 to 4 C atoms.

As naturally occurring hydroxycarboxylic acids with 2 to 6 C atoms, one can, for example, mention the following: glycolic acid, β -hydroxybutyric acid, α -hydroxyisovaleric acid, α -hydroxy- α -methylvaleric acid, α -hydroxy- γ -methylvaleric acid, α -hydroxycaproic acid, and β -hydroxycaproic acid, in particular, however, lactic acid.

As carboxylic acids that have 1 to 4 C atoms, with which the hydroxy group of the hydroxycarboxylic acids can be esterified, one can mention, above all, formic acid, acetic acid, and propionic acid.

The esters to be used in accordance with the invention are, only in part, novel. Of the esters described, however, it was unknown that they exert a physiological cooling effect on the skin and mucous membranes of the body. The esters can be produced according to traditional methods, for example, by the acid-catalyzed esterification of methanol with hydroxycarboxylic acids or by the reduction of menthyl ketocarboxylates. The menthyl ketocarboxylates can, in turn, be obtained, for example, by the transesterification of alkyl ketocarboxylates with menthol. The esterification of the hydroxy group of the hydroxycarboxylic acid with carboxylic acids that have 1 to 4 C atoms is appropriately carried out as the last stage.

The esters to be used in accordance with the invention have asymmetrical C atoms; optical isomerism can therefore appear with their use. Depending on the starting material and the production methods, used they can be present as mixtures of the optical isomers or as pure isomers. The cooling effect of the isomers can be different, so that one or another isomer may be preferred.

The cooling agents in accordance with the invention can be used anywhere that a physiological cooling effect is desired. Compositions in which such cooling agents are preferably used are, for example, consumption articles with little or no food value, such as chewing gum, chewing tobacco, cigarettes, beverages, ice cream, candies, and so forth, pharmaceutical

preparations, body care agents, or cosmetic preparations, such as tooth care agents, mouthwash, gargling preparations, perfumes, powders, lotions, ointments, gels, creams, shaving lotions, shampoos, etc.

The end products contain the esters to be used in accordance with the invention, in a quantity that is sufficient to stimulate the cold receptors and to produce the desired cold sensitivity. As a rule, 0.1 to 5 weight-percent, with reference to the weight of the total composition, is used. In addition to the cooling effect, the esters in accordance with the invention, in particular, the menthyl lactate, exhibit an enhancing effect--that is, a taste-reinforcing effect for other flavorings. For example, the addition of a quantity of ester to be used in accordance with the invention, which is also below the threshold for a physiological cooling effect, reduces the quantity of peppermint oil, spearmint oil, or other flavorings incorporated, for example, into the chewing gum or dentomints as flavorings, without a deviation of the taste occurring.

The following examples explain the use of the cooling agents in accordance with the invention and in different compositions. The indications of percentages are weight-percent unless indicated otherwise.

EXAMPLE 1

Toothpaste

The following components were mixed in the usual manner

Glycerol, Pharmacopoeia 6	20%
Methyl p-hydroxybenzoate	0.15%
Carboxymethylcellulose	1.2%
Saccharin	0.2%
Dicalcium phosphate (water-containing)	48%
Sodium lauryl sulfate	2.2%
Flavorings	1.0%
Water	100%

Before the mixing process had ended, 1% of 1-menthyl lactate was added. The toothpaste was characterized by a cooling effect.

EXAMPLE 2

Chewing gum

0.3% of 1-menthyl-O-acetyl lactate was worked into a commercial chewing gum base. The chewing gum mass produced a cooling feeling in the mouth.

EXAMPLE 3**Fondant**

1% of 1-menthyl lactate was worked into a commercial fondant base. The fondant mass had a pleasant refreshing taste.

EXAMPLE 4**Mouthwash**

A mouthwash concentrate was produced from the following components:

Ethanol	60%
Bromochlorophene	0.05%
Polyoxyethylene sorbitan monolaurate	1%
Allantoin	0.2%
Saccharin	0.2%
Flavorings	to 100%

5% of 1-menthyl lactate was added to the mixture. For the production of a mouthwash, the concentrate was diluted with a 10-fold volume of water. The mouthwash was characterized by a cooling effect.

A similarly acting mouthwash was obtained when, instead of 5% of 1-menthyl lactate, the same quantity of 1-menthyl glycolate, β -hydroxybutyrate, α -hydroxyisovalerate, α -hydroxy- α -methylvalerate, α -hydroxy- γ -methylvalerate, α -hydroxycaproate, or β -hydroxycaproate was used.

EXAMPLE 5**Face cleansing lotion**

A face cleansing lotion was produced from the following components:

Ethanol	26.3%
1-Menthyl lactate	1%
Perfume oil	0.1%
Emulsifier	4%
1,2-Propylene glycol	1%
Allantoin	0.05%
Lactic acid	0.05%
Water	67.5%

The lotion produced a cooling effect on facial skin.

EXAMPLE 6

After-shave lotion

An after-shave lotion was produced from the following components

Ethanol	55.5%
1-Menthyl lactate	1.5%
Perfume oil	0.5%
Emulsifier	0.3%
Water	39.8%
Allantoin	0.2%
1,2-Propylene glycol	2%
Lactic acid	0.2%

The lotion produced a cooling effect on the face upon application.

A similarly acting preparation was obtained when, instead of 1-menthyl lactate, the same quantity of 1-menthyl-O-formyl lactate was used.

EXAMPLE 7

Clear shampoo

A clear shampoo was produced from the following components:

Fatty acid amidoalkylbetaine	60%
Water	35.2%
Preservative	0.2%
d,1-Menthyl lactate	2%
Perfume oil	0.5%
Cocofatty acid diethanol amide	2%

The shampoo produced a cooling effect on the scalp.

EXAMPLE 8

After-bath freshener

An after-bath freshener was produced from the following components:

Ethanol	50%
1-Menthyl lactate	1.5%
Perfume oil	2%

Oil-replenishing agent based on lanolin	2%
Emulsifier	1.5%
Water	43%

The after-bath freshener was characterized by a pleasant, refreshing effect.